

REMARKS

This amendment is responsive to the final Office Action mailed October 21, 2002. Claims 98-112, 114-117 and 121 were pending in the instant Application. In this amendment, Claims 98-112, 114-117, and 121 are cancelled without prejudice to Applicants' right to pursue the subject matter of the cancelled claims in one or more related continuation, divisional or continuation-in-part application(s) and new Claims 122-150 are presented. Thus, following entry of the present amendment, Claims 122-150 will be pending and under consideration.

I. The Amendment to the Claims

In the present amendment, Claims 98-112, 114-117, and 121 are cancelled and new Claims 122-150 are presented for examination. New Claims 122-150 are fully supported by the specification and claims of the application as originally filed.

In particular, support for new Claim 122 can be found, for example, in Claims 98 and 100 as originally filed and in the specification at page 60, lines 1-17 and lines 25-29, and at page 94, lines 26-32. Support for new Claim 123 can be found, for example, in Claim 99 as originally filed and in the specification at page 60, lines 18-23. Support for new Claim 124 can be found, for example, in Claim 107 as originally filed and at page 164, line 28 to page 165, line 3. Support for new Claim 125 can be found, for example, in Claim 109 as originally filed and in the specification at page 165, lines 11-15 and page 189, Table 27. Support for new Claim 126 can be found, for example, in Claim 117 as originally filed and in the specification at page 167, lines 11-28, and at page 94, lines 26-32.

Support for new Claim 127 can be found, for example, in Claim 98 as originally filed and in the specification at page 60, lines 1-17, and at page 94, lines 26-32. Support for new Claim 128 can be found, for example, in Claim 99 as originally filed and in the specification at page 60, lines 18-23. Support for new Claim 129 can be found, for example, in Claim 100 as originally filed and in the specification at page 60, lines 25-29. Support for new Claim 130 can be found, for example, in Claim 101 as originally filed and in the specification at page 163, lines 2-19. Support for new Claim 131 can be found, for example, in Claim 102 as originally filed and in the specification at page 163, lines 21-29. Support for new Claim 132 can be found, for example, in Claim 104 as originally filed and in the specification at page 164, lines 7-11.

Support for new Claim 133 can be found, for example, in Claim 105 as originally filed and in the specification at page 164, lines 13-19. Support for new Claim 134 can be

found, for example, in Claim 107 as originally filed and in the specification at page 164, line 28, to page 165, line 3. Support for new Claim 135 can be found, for example, in Claim 109 as originally filed and in the specification at page 165, lines 11-15. Support for new Claim 136 can be found, for example, in Claim 110 as originally filed and in the specification at page 165, lines 17-25. Support for new Claim 137 can be found, for example, in Claim 112 as originally filed and in the specification at page 166, lines 1-10. Support for new Claim 138 can be found, for example, in Claim 117 as originally filed and in the specification at page 167, lines 11-28, and at page 94, lines 26-32.

Support for new Claim 139 can be found, for example, in Claims 98, 103, and 106 as originally filed and in the specification at page 60, lines 1-17, and page 94, lines 26-32. Support for new Claim 140 can be found, for example, in Claim 99 as originally filed and in the specification at page 60, lines 18-23. Support for new Claim 141 can be found, for example, in Claim 100 as originally filed and in the specification at page 60, lines 25-29. Support for new Claim 142 can be found, for example, in Claim 101 as originally filed and in the specification at page 163, lines 2-19. Support for new Claim 143 can be found, for example, in Claim 103 as originally filed and in the specification at page 163, line 31 to page 164, line 4.

Support for new Claim 144 can be found, for example, in Claim 104 as originally filed and in the specification at page 164, lines 7-11. Support for new Claim 145 can be found, for example, in Claim 106 as originally filed and in the specification at page 164, lines 21-26. Support for new Claim 146 can be found, for example, in Claim 107 as originally filed and in the specification at page 164, line 28, to page 165, line 3. Support for new Claim 147 can be found, for example, in Claim 109 as originally filed and in the specification at page 165, lines 11-15. Support for new Claim 148 can be found, for example, in Claim 111 as originally filed and in the specification at page 165, lines 27-33. Support for new Claim 149 can be found, for example, in Claim 117 as originally filed and in the specification at page 94, lines 26-32; page 167, lines 11-29; and at page 169, lines 17-23. Finally, support for new Claim 150 can be found, for example, in Claim 121 as originally filed and in the specification at page 89, line 7 to page 93, line 29, particularly at page 91, line 34 to page 95, line 24.

Further support for new Claims 122-150 is provided by Claims 98, 101-107, 109-112, 114-117, and 121 as amended in the amendment filed July 15, 2002. These amendments to Claims 98, 101-107, 109-112, 114-117, and 121 were entered without objection in the Office

Action mailed October 21, 2002, indicating that the PTO considered this amendment to be fully supported by the application as filed.

Applicants note that Claims 127-138 recite groups of secondary mutations that are smaller than the groups of secondary mutations recited by the claims as originally filed. For example, Claim 127 recites a reduced group of secondary mutations in comparison to Claim 98 as originally filed. Although the groups of secondary mutations are reduced in number, each member of each group of secondary mutations presented by the new claims is recited in a single group by the specification and at least one claim. Thus, the reduced groups of secondary mutations recited by Claims 127-138 are supported by the larger sets of secondary mutations described in the application as originally filed.

In support of Applicants' contention that the larger groups of secondary mutations recited by the as-filed claims provide adequate description for the claims presented in the instant amendment, Applicants respectfully invite the PTO's attention to M.P.E.P.

§ 2173.05(i). Here, the M.P.E.P. explains that "[i]f alternative elements are positively recited in the specification, they may be explicitly excluded in the claims." See M.P.E.P.

§ 2173.05(i). The legal basis for this rule is found in *In re Johnson* 558 F.2d 1008, 194

U.S.P.Q. 187 (C.C.P.A., 1977). In *In re Johnson*, the Applicants described a genus of chemical compounds in the application as filed, then claimed a subgenus of the compounds that lacked word-for-word support in the application as filed. The Court of Customs and

Patent Appeals held that "the specification, having described the whole [genus], necessarily

described the [subgenus] remaining." See *In re Johnson* 558 F.2d 1008, 1019, 194 U.S.P.Q.

187, 196 (C.C.P.A., 1977). Thus, Applicants respectfully submit that *In re Johnson* and

M.P.E.P. § 2173.05(i) show that the larger groups of secondary mutations described by the application as filed support the smaller groups of secondary mutations recited by Claims 127-138 as presented in the instant amendment.

In view of the foregoing, Applicants respectfully submit that new Claims 122-150 are fully supported by the specification and claims of the application as originally filed.

Accordingly, no new matter is introduced by the instant amendment. Therefore, Applicants hereby respectfully request entry of the present amendment under 37 C.F.R. § 1.116.

Applicants believe that the present amendment is suitable for entry under 37 C.F.R. § 1.116 because it places the claims in condition for allowance and because no new search would be required to examine the subject matter of the present claims. Accordingly, Applicants earnestly request that the present amendment be entered into the record of the present application.

II. The Rejection of Claims 98-112, 114-117, and 121 under 35 U.S.C. § 112, Second Paragraph

Claims 98-112, 114-117, and 121 stand rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite. In particular, the PTO asserts that Claims 98-112, and 114-117 are indefinite because the phrase drawn to the presence of a specific mutation indicating a change in susceptibility is unclear in that a change would only be recognized if the sample is compared to a previous sample from the same patient. Further, Claim 121 is asserted to be indefinite because the recited mutations are already known to be present, such that it is unnecessary for the claimed vector to comprise an indicator gene.

By way of response and without acquiescing to the propriety of the rejection, Applicants respectfully submit that the rejection of method Claims 98-112, 114-117, and 121 as indefinite is moot in view of the cancellation of Claims 98-112, 114-117, and 121, and the introduction of new method Claims 122-149, which each recite that susceptibility of the HIV protease encoded by the recited nucleic acid to a protease inhibitor is different relative to a reference HIV protease. The specification at page 94, lines 25-32, makes clear that the reference HIV protease can, for example, include control HIV proteases from a database or an HIV protease from a sample taken from the patient prior to initiation of therapy. Accordingly, one of skill in the art can readily understand the scope of new Claims 122-149.

Further, one of skill in the art can also understand the metes and bounds of new Claim 150. New Claim 150 recites a test vector that comprises two elements, a patient-derived nucleic acid segment encoding a HIV protease having certain mutations and an indicator gene, the amount of expression of which depends on the protease activity encoded by the HIV protease segment. New Claim 150 does not recite that expression of the indicator gene depends on the presence or absence of any particular mutations. Thus, the ordinarily skilled artisan can recognize the metes and bounds of Claim 150 as currently pending.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph, be withdrawn..

III. The Rejection of Claims 98-102, 104, 105, 107-110, 112, and 114-117 under 35 U.S.C. § 102(b)

Each of Claims 98-102, 104, 105, 107-110, 112, and 114-117 stands rejected under 35 U.S.C. § 102(b) as allegedly anticipated by one of two references. In particular, Claims 98-102, 104, 105, 107, 108, 112, and 114-117 stand rejected as allegedly anticipated by Young *et al.*, 1998, *J. Infect. Dis.* 178:1497-1501 ("*Young*"), while Claims 98-100 and 107-109 stand rejected as allegedly anticipated by Hertogs *et al.*, 1998, *Antimicrob. Agents*

Chemother. 42:269-276 (“*Hertogs*”). In response, Applicants respectfully submit the rejection is moot in view of the cancellation of the rejected claims, and further submit that the cited references do not teach each and every element of the invention as recited by new Claims 122-149. Thus, neither *Young* nor *Hertogs* anticipates new Claims 122-149.

A. The Legal Standard for Anticipation

The standard governing anticipation under 35 U.S.C. § 102 requires strict identity. See M.P.E.P. § 2131. Thus, “for a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference.” See *In re Bond*, 15 U.S.P.Q.2d 1566 (Fed. Cir., 1990). Anticipation is not shown even when the differences between the claims and the cited reference are allegedly “insubstantial” and any missing elements could be supplied by the knowledge of one skilled in the art. See *Structural Rubber Prod. Co. v. Park Rubber Co.*, 223 U.S.P.Q. 1264 (Fed. Cir., 1984). Furthermore, in *Jamesbury Corp. v. Litton Industrial Products, Inc.*, 225 U.S.P.Q. 253 (Fed. Cir., 1985), the Federal Circuit explained that even if the prior art teaches “substantially the same thing” as the claimed invention, the reference still cannot anticipate the invention. Thus, a cited reference must describe each and every claim limitation in order to anticipate the invention as claimed.

B. The Cited References do not Teach Each and Every Element of the Invention as Presently Claimed

Neither *Young* nor *Hertogs* teaches or suggests any of the methods recited by Claims 122-149. In particular, neither *Young* nor *Hertogs* teaches or suggests any methods relating to assessing the effectiveness of amprenavir-based HIV therapy as recited by new Claims 122-126. Both *Young* and *Hertogs* discuss the phenotypes and genotypes of HIV strains isolated from patients that had been treated with one or more protease inhibitors, including indinavir, ritonavir, and saquinavir. Neither *Young* nor *Hertogs* discuss amprenavir or methods of assessing increased or decreased amprenavir susceptibility by detecting mutations in particular codons that are correlated with such changed susceptibility. Further, neither *Young* nor *Hertogs* discusses whether the same mutations that alter susceptibility to other protease inhibitors may affect susceptibility to amprenavir. Accordingly, neither *Young* nor *Hertogs* teaches or suggests any of Claims 122-126.

Moreover, neither *Young* nor *Hertogs* teaches or suggests any methods relating to assessing the effectiveness of protease inhibitor antiviral therapy comprising detecting any of the codons recited by new Claims 127-138. *Young* and *Hertogs* teach several codons,

mutations of which are alleged to correlate with resistance to one or more protease inhibitors. However, none of these codons is presently recited as an acceptable secondary mutation for assessing the effectiveness of protease antiretroviral therapy by any of Claims 127-138. Further, neither *Young* nor *Hertogs* provides any guidance or suggestion for identifying the secondary mutation codons recited by Claims 127-138 from the lists of codons taught therein. Accordingly, neither *Young* nor *Hertogs* teaches or suggests the methods for assessing the effectiveness of protease antiretroviral therapy recited by Claims 127-138.

Finally, neither *Young* nor *Hertogs* teaches or suggests methods for assessing the effectiveness of protease inhibitors wherein the susceptibility of HIV to the antiretroviral treatment is increased rather than decreased as recited by Claims 139-149. *Young* and *Hertogs* discuss mutations in specific codons that result in resistance to protease inhibitors. In the Office Action mailed October 21, 2002, the PTO states that the mutations presented in Table 1 of *Young* result in increased sensitivity to indinavir and saquinavir; Applicants respectfully suggest that the PTO has misread the table legend. In fact, *Young* states that these mutations correlate with drug resistance rather than increased drug sensitivity. In no way do *Young* or *Hertogs* teach or suggest mutations in specific codons that result in increased susceptibility of HIV to protease inhibitors as recited by Claims 139-149. Thus, neither *Young* nor *Hertogs* can teach or suggest the methods for assessing the effectiveness of protease antiretroviral therapy recited by Claims 139-149.

As shown by the foregoing, neither *Young* nor *Hertogs* teaches or suggests each element of the methods of assessing the effectiveness of protease antiretroviral therapy in patients by detecting mutations at certain codons of the gene encoding HIV protease in viral nucleic acids recited by Claims 122-149. Accordingly, *Young* and *Hertogs*, either alone or in combination, do not anticipate or render obvious Claims 122-149 under 35 U.S.C. § 102(b).

IV. The Rejection of Claim 121 as Obvious under 35 U.S.C. § 103(a)

Claim 121 stands rejected as obvious over *Hertogs* in view of U.S. Patent No. 5,837,464 ("the '464 patent"). Without acquiescing to the propriety of the rejection, Applicants respectfully submit that the rejection of Claim 121 is moot in view of its cancellation. Further, Applicants respectfully submit that new Claim 150 is not obvious over *Hertogs* in view of the '464 patent because the cited references, either alone or in combination, do not teach or suggest each and every element of the invention of Claim 150.

A. The Legal Standard

To reject a claim as under 35 U.S.C. § 103(a), the PTO bears the initial burden of showing an invention to be prima facie obvious over the prior art. *See In re Bell*, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1992). If the PTO cannot establish a prima facie case of unpatentability, then without more the applicant is entitled to grant of the patent. *See In re Oetiker*, 24 U.S.P.Q.2d 1443 (Fed. Cir. 1992). The PTO must meet a three-part test to render a claimed invention prima facie obvious.

To begin with, the prior art references cited by the PTO must provide “motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant.” *See In re Kotzab*, 55 U.S.P.Q.2d 1316 (Fed. Cir. 2000). Where one reference is relied upon by the PTO, there must be a suggestion or motivation to modify the teachings of that reference. *See id.* Where an obviousness determination rests or relies on the combination of two or more references, there must be some suggestion or motivation to combine the references. *See WMS Gaming Inc. v. International Game Technology*, 51 U.S.P.Q.2d 1386 (Fed. Cir. 1999). The suggestion may be found in implicit or explicit teachings within the references themselves, from the ordinary knowledge of one skilled in the art, or from the nature of the problem to be solved. *See id.*

Second, the prior art references cited by the PTO must suggest to one of ordinary skill in the art that the invention would have a reasonable expectation of success. *See In re Dow Chemical*, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988). The expectation of success, like the motivation to combine two prior art references, must come from the prior art, not the applicant’s disclosure. *See id.*

Finally, the PTO must show that the prior art references, either alone or in combination, teach or suggest each and every limitation of the rejected claims. *See In re Gartside*, 53 U.S.P.Q.2d 1769 (Fed. Cir. 2000). If any one of these three factors is not met, the PTO has failed to establish a prima facie case of obviousness and the applicant is entitled to grant of a patent without making any affirmative showing of non-obviousness.

B. Hertogs in Combination with the '464 Patent do not Teach or Suggest Each and Every Element of the Invention

Claim 150 recites a test vector comprising an indicator gene and a segment derived from an HIV-infected patient that further comprises a protease-encoding nucleic acid that has a mutation at codon 82 and a secondary mutation at codon 73, 55, 53, 23, 33, or 59, or a mutation at codon 90 and a secondary mutation at codon 53, 95, 55, 85, 66, 33, 73, 23, or 58. Neither *Hertogs* nor the '464 patent, either alone or in combination, teach or suggest a test

vector comprising protease-encoding nucleic acid that has a mutation at codon 82 or at codon 90 in combination with any of the recited secondary mutations. Thus, an element of Claim 150 is neither taught nor suggested by the cited references, and therefore the PTO cannot make a *prima facie* case of obviousness of Claim 150. Accordingly, Applicants respectfully submit that Claim 150 is not obvious under 35 U.S.C. § 103(a) and earnestly request passage of the new claims to issuance.

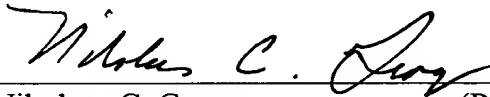
CONCLUSION

In light of the above amendments and remarks, Applicants respectfully submit that Claims 122-150 satisfy all the criteria for patentability and are in condition for allowance. Accordingly, Applicants respectfully request that the Examiner reconsider this application with a view towards allowance and solicit an expeditious passage of Claims 122-150 to issuance. The Examiner is invited to call the undersigned attorney at (212) 790-9090, if a telephone call could help resolve any remaining items.

Pursuant to 37 CFR § 1.136(a)(3), the Commissioner is authorized to charge all required fees, fees under 37 CFR § 1.17 and all required extension of time fees, or credit any overpayment, to Pennie & Edmonds, LLP U.S. Deposit Account No. 16-1150 (order no. 011068-0033-999).

Respectfully submitted,

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